



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: BALDWIN *et al.*

Serial No.: 09/391,783

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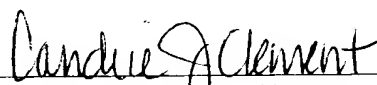
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Date of Signature: December 3, 2002

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**RESPONSE TO REQUIREMENT for ELECTION of SPECIES UNDER 37 CFR §1.121**

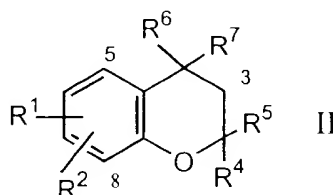
Dear Sir:

This is a reply to the Office communication mailed June 3, 2002 (paper number 14), which set a one month period for response. In light of the accompanying fee and request for an extension of time, a reply to the Action is due December 3, 2002, and this response is timely filed.

In light of a previous requirement for restriction and a subsequent amendment to add claims 39-49, claims 4-7 and 38-49 are pending in the application. The present Office Action requires Applicants to elect a single disclosed species for prosecution on the merits, to which the claims shall be restricted if no generic claim is found allowable. More specifically, the Action requires Applicants to "elect, **for purposes of a search**, a single, fully-defined compound. That is, all atoms and bonds of each and every variable group should be defined. . . . The instant species election requires that one - and only one- compound be elected; the elected species should contain no variable groups."

With regard to an election of species, Applicants elect the species defined as:

A compound of the formula:



wherein:

$R^1$  is  $-OCH_2CO_2H$ ;

$R^2$  is  $-H$ ;

$R^4$  and  $R^5$  taken together are  $-(CH_2)_2-S(O)_{0-2}-(CH_2)_2-$ ;

one of  $R^6$  and  $R^7$  is  $-H$  and the other is  $-H$  or  $-N(CH_2)_{1-6}R^{14}R^{15}$ ;

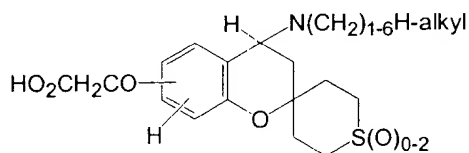
$R^{14}$  is  $-H$ ; and

$R^{15}$  is alkyl,

or a pharmaceutically acceptable salt thereof.

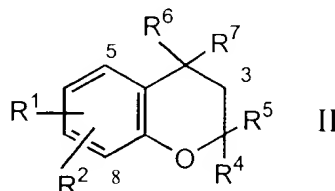
As required, each of the variables in generic Formula II, *i.e.*,  $R^1$  through  $R^7$ , has been defined. With respect to the definition of  $R^6$  and  $R^7$ , the variables  $R^{14}$  and  $R^{15}$ , have also been defined.

The elected species is represented by the structure:



The elected variable definitions are underlined and bolded in the following copy of generic claim 4.

4. A compound of the formula:



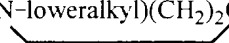
wherein:

**R<sup>1</sup>** is OH, O(CH<sub>2</sub>)<sub>1-2</sub>OH, **OCH<sub>2</sub>CO<sub>2</sub>H**, CO<sub>2</sub>H, O-Z-C(O)NH(CH<sub>2</sub>)<sub>1-6</sub>R<sup>17</sup> or OCH<sub>2</sub>-4-Phe-C(O)NH(CH<sub>2</sub>)<sub>1-6</sub>R<sup>17</sup>;






**R<sup>2</sup>** is **H** or lower alkyl;


R<sup>3</sup> is H, alkyl, aryl, or arylalkyl;

R<sup>4</sup> and R<sup>5</sup> are each independently H, lower alkyl, or substituted lower alkyl where the substituents are 1-3 alkoxy, aryl, substituted aryl, carboalkoxy, carboxamido or di-loweralkylamido; or

**R<sup>4</sup> and R<sup>5</sup> taken together are** -(CH<sub>2</sub>)<sub>n</sub>-, -(CH<sub>2</sub>)<sub>2</sub>-O-(CH<sub>2</sub>)<sub>2</sub>-, -CH<sub>2</sub>-O-(CH<sub>2</sub>)<sub>3</sub>-,  
-(CH<sub>2</sub>)<sub>2</sub>-NR<sup>8</sup>-(CH<sub>2</sub>)<sub>2</sub>-, -CH<sub>2</sub>-NR<sup>8</sup>-(CH<sub>2</sub>)<sub>m</sub>-, -(CH<sub>2</sub>)<sub>2</sub>CH(NHR<sup>8</sup>)(CH<sub>2</sub>)<sub>2</sub>-,  
-CH<sub>2</sub>CH(N-loweralkyl)(CH<sub>2</sub>)<sub>2</sub>CHCH<sub>2</sub>-,  
**-(CH<sub>2</sub>)<sub>2</sub>-S(O)<sub>0-2</sub>-(CH<sub>2</sub>)<sub>2</sub>-**, or  ;

**one of R<sup>6</sup> and R<sup>7</sup> is H and the other is H, OH, or N(CH<sub>2</sub>)<sub>1-6</sub>R<sup>14</sup>R<sup>15</sup>;** or

R<sup>6</sup> and R<sup>7</sup> taken together are , , ,  or , with the proviso that when

R<sup>1</sup> is -OH and R<sup>2</sup> is -H, R<sup>6</sup> and R<sup>7</sup> are not -H and -OH or when taken together are not  ;

R<sup>8</sup> is H, COOR<sup>9</sup>, CONHR<sup>10</sup>, CSNHR<sup>11</sup>, COR<sup>12</sup>, SO<sub>2</sub>R<sup>13</sup>, lower alkyl, aryl lower alkyl, heteroaryl, or heteroaryl lower alkyl, wherein aryl is optionally substituted with 1-3 substituents selected from lower alkyl, lower alkoxy, halo, CN, NH<sub>2</sub>, COOH, CONH<sub>2</sub>, carboalkoxy, and mono- or di-lower alkylamino and wherein heteroaryl is a mono- or bicyclic heteroaromatic ring system of 5 to 10 members including 1 to 3 heteroatoms selected from O, N, and S and 0-3 substituents selected from halo, amino, cyano, lower alkyl, carboalkoxy, CONH<sub>2</sub>, and S-lower alkyl;

- $R^9$  is lower alkyl, aryl, aryl lower alkyl, heteroaryl, aryl substituted by 1-3 substituents selected from alkyl, alkenyl, alkoxy, methylene dioxy, and halo, or a 5- to 6-membered heterocyclic ring containing O or N as a heteroatom, wherein heteroaryl is a heteroaromatic ring of 5 to 6 members including 1 to 2 heteroatoms selected from O, N, and S and 0-2 substituents selected from lower alkyl, dialkylamino, lower alkoxy, and halo;
- $R^{10}$  and  $R^{11}$  are each independently lower alkyl, aryl, aryl lower alkyl, or aryl substituted by 1-3 substituents selected from lower alkyl, halo, alkoxy and haloalkyl;
- $R^{12}$  is lower alkyl, aryl, heteroaryl, aryl lower alkyl, heteroaryl lower alkyl, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from O, S, and N, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from O, S, and N-lower alkyl, or aryl substituted with 1-3 substituents selected from lower alkyl, alkoxy, halo, sulfamoyl, lower alkyl sulfamoyl, cyano, and phenyl;
- $R^{13}$  is lower alkyl, aryl, or aryl substituted with 1-3 substituents selected from lower alkyl, alkoxy, halo, CN, and haloalkyl;
- $R^{14}$  is H;** alkyl; alkyl substituted by 1-3 alkoxy, S-lower alkyl, sulfamoyl, halo, alkylsulphonamido, or arylsulphonamido; alkenyl; alkynyl; aryl; substituted aryl; heteroaryl; substituted heteroaryl; heterocycloalkyl;  $-\text{CH}_2\text{NR}^{16}\text{C}(\text{O})\text{R}^{16}$ ;  $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{16}$ ;  $-\text{CH}_2\text{OC}(\text{O})\text{R}^{16}$ ; or  $-\text{CH}_2\text{SC}(\text{O})\text{R}^{16}$ ;
- $R^{15}$  is H, alkyl,**  $-\text{C}(\text{O})\text{X}$ ,  $-\text{C}(\text{S})\text{X}$ , or  $-\text{C}(\text{NCN})\text{NR}^3\text{R}^3$ ;
- $R^{16}$  is lower alkyl, substituted lower alkyl, aryl, or substituted aryl;
- $R^{17}$  is H; alkyl; alkyl substituted by 1-3 alkoxy, S-lower alkyl, sulfamoyl, halo, alkylsulphonamido, or arylsulphonamido; alkenyl; alkynyl; aryl; substituted aryl; heteroaryl; substituted heteroaryl; heterocycloalkyl;  $-\text{CH}_2\text{NR}^{16}\text{C}(\text{O})\text{R}^{16}$ ;  $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{16}$ ;  $-\text{CH}_2\text{OC}(\text{O})\text{R}^{16}$ ; or  $-\text{CH}_2\text{SC}(\text{O})\text{R}^{16}$ ;
- X is alkyl, aryl, arylalkyl, O-loweralkyl, or  $-\text{NR}^3\text{R}^3$ ;
- Z is  $-(\text{CH}_2)_{1-6}-$ , optionally substituted with 1-3 lower alkyl;  $-\text{CHR}^2-$ ;  $-\text{Phe}-\text{CH}_2-$ , where Phe is optionally mono-substituted with halogen, lower alkyl, or alkoxy; or heteroarylene- $(\text{CH}_2)-$ ;
- m is 2 or 3; and
- n is 4-9;
- or a pharmaceutically acceptable salt thereof.

With regard to the remaining pending claims, claims 38-39 and 41 read on the elected species.

Respectively submitted,

December 3, 2002



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